

IN THE ABSTRACT:

Please add the Abstract of the Disclosure at page 61 as follows:

ABSTRACT OF THE DISCLOSURE

H¹
The invention relates to processes for producing an immunoglobulin or an immunologically functional immunoglobulin fragment containing at least the variable domains of the immunoglobulin heavy and light chains. The processes can use one or more vectors which produce both the heavy and light chains or fragments thereof in a single cell. The invention also relates to the vectors used to produce the immunoglobulin or fragment, and to cells transformed with the vectors.

IN THE SPECIFICATION:

Please add a paragraph beginning at page 1, before line 12 as follows:

H²
--Cross-reference to Related Applications

This application is a continuation of U.S. Application Serial No. 06/483,457, filed April 8, 1983, now U.S. Patent No. 4,816,567, issued March 28, 1989.--

IN THE CLAIMS:

Please cancel Claims 133-134.

Please replace Claims 101, 104, 108-111, 115, 118, 121, 122, 127-130 and 132, and add new Claims 135-138, as follows:

H³
1¹ 101. (Amended) A process for producing an immunoglobulin molecule or an immunologically functional immunoglobulin fragment comprising at least the variable domains of the immunoglobulin heavy and light chains, in a single host cell, comprising the steps of:

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(i) transforming said single host cell with a first DNA sequence encoding at least the variable domain of the immunoglobulin heavy chain and a second DNA sequence encoding at least the variable domain of the immunoglobulin light chain, and

(ii) independently expressing said first DNA sequence and said second DNA sequence so that said immunoglobulin heavy and light chains are produced as separate molecules in said transformed single host cell.

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4 104. (Amended) A process according to claim 103 wherein the vector is a plasmid.

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108. (Amended) A process according to claim 107 wherein the host cell is *E. coli* strain X1776 (ATCC No. 31537).

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109. (Amended) A process according to claim 101 wherein the immunoglobulin heavy and light chains are expressed in the host cell and secreted therefrom as an immunologically functional immunoglobulin molecule or immunoglobulin fragment.

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110. (Amended) A process according to claim 101 wherein the immunoglobulin heavy and light chains are produced in insoluble form and are solubilized and allowed to refold in solution to form an immunologically functional immunoglobulin molecule or immunoglobulin fragment.

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111. (Amended) A process according to claim 101 wherein the DNA sequences code for the complete immunoglobulin heavy and light chains.

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115. (Amended) A vector comprising a first DNA sequence encoding at least a variable domain of an immunoglobulin heavy chain and a second DNA sequence encoding at least a variable domain of an immunoglobulin light chain wherein said first DNA sequence and said second DNA sequence are located in said vector at different insertion sites.

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118. (Amended) A transformed host cell comprising at least two vectors, at least one of said vectors comprising a DNA sequence encoding at least a variable domain of an immunoglobulin heavy chain and at least another one of said vectors comprising a DNA sequence encoding at least the variable domain of an immunoglobulin light chain.

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121. (Amended) A method comprising

- a) preparing a DNA sequence consisting essentially of DNA encoding an immunoglobulin [selected from the group] consisting of an immunoglobulin heavy chain and light chain or Fab region, said immunoglobulin having specificity for a particular known antigen;
- b) inserting the DNA sequence of step a) into a replicable expression vector operably linked to a suitable promoter;
- c) transforming a prokaryotic or eukaryotic microbial host cell culture with the vector of step b);
- d) culturing the host cell; and
- e) recovering the immunoglobulin from the host cell culture, said immunoglobulin being capable of binding to a known antigen.

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122. (Amended) The method of claim 121 wherein the heavy and light chain are the heavy and light chains of anti-CEA antibody.

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127. (Amended) The method of claim 126 wherein the heavy chain and light chains or Fab region are deposited within the cells as insoluble particles.

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128. (Amended) The method of claim 127 wherein the heavy and light chains are recovered from the particles by cell lysis followed by solubilization in denaturant.

H9 ²⁹ ~~129~~. (Amended) The method of claim ²¹ ~~121~~ wherein the heavy and light chains are secreted into the medium.

³⁰ ~~130~~. (Amended) The method of claim ²¹ ~~121~~ wherein the host cell is a gram negative bacterium and the heavy and light chains are secreted into the periplasmic space of the host cell bacterium.

H10 ³² ~~132~~. (Amended) The insoluble particles of heavy chain and light chains or Fab region produced by the method of claim ²⁷ ~~127~~.

H11 ³³ ~~135~~. (New) A process for producing an immunoglobulin molecule or an immunologically functional immunoglobulin fragment comprising at least the variable domains of the immunoglobulin heavy and light chains, in a single host cell, comprising:
independently expressing a first DNA sequence encoding at least the variable domain of the immunoglobulin heavy chain and a second DNA sequence encoding at least the variable domain of the immunoglobulin light chain so that said immunoglobulin heavy and light chains are produced as separate molecules in said single host cell transformed with said first and second DNA sequences.

³⁴ ~~136~~. (New) The process of Claim ⁹ ~~109~~, further comprising the step of attaching the immunoglobulin molecule or immunoglobulin fragment to a label or drug.

³⁵ ~~137~~. (New) The process of Claim ¹⁰ ~~110~~, further comprising the step of attaching the immunoglobulin molecule or immunoglobulin fragment to a label or drug.

³⁶ ~~138~~. (New) The process of Claim ³³ ~~135~~, further comprising the step of attaching the immunoglobulin molecule or immunoglobulin fragment to a label or drug.